REMARKS

Applicants have received and reviewed the Final Office Action mailed June 5, 2002. Claims 2, 3 and 33-48 are currently pending in the referenced application, all of which were rejected. Applicants herein propose to amend claims 2, 33, 35, 37, 40, 43, and 46 and, to the extent necessary, renew their request to cancel claims 1 and 9-11. All claim amendments and cancellations herein are made without prejudice or disclaimer. Applicants respectfully request reconsideration of the application as proposed to be amended herein.

Claims 1 and 9-11

1. It is indicated in the Office Action that claims 1 and 9-11 remain pending in the application. Applicants respectfully direct the Office's attention to the "VERSION WITH MARKINGS TO SHOW CHANGES MADE" submitted with the Amendment filed herein on February 28, 2002, where cancellation of claims 1 and 9-11 is requested. To the extent said amendment was not effective to cancel claims 1 and 9-11, applicants kindly request the Office to cancel claims 1 and 9-11 without prejudice or disclaimer.

Anticipation Rejection based on Crystal *et al.*

2. The Office maintained the rejection of claims 1, 9 and 11 under 35 U.S.C. § 102(e) as being anticipated by Crystal *et al.* (U.S. Patent 6,127,525). This rejection is moot in view of the cancellation of the subject claims. Accordingly, withdrawal of the rejection is respectfully solicited.

Obviousness Rejection based on Crystal *et al.* in view of Wickham *et al.*

3. Claims 2, 3, 10, and 33-48 were newly rejected under 35 U.S.C. § 103(a) as being unpatentable over Crystal in view of Wickham *et al.* (U.S. Patent 5,770,442). The rejection with respect to claim 10 is moot in view of the cancellation of that claim. Applicants respectfully traverse the rejection with respect to claims 2, 3, and 33-48 for the reasons set forth below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. (*See* MPEP § 706.02(j)). First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify

the reference or combine reference teachings; second, there must be a reasonable expectation of success; and third, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (*Id.*). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicants' disclosure. (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

The Proposed Combination Does Not Teach All Claim Limitations

Applicants first respectfully submit the proposed combination fails to teach or suggest each and every limitation of the subject claims and, accordingly, fails to render the subject claims obvious. Applicants respectfully disagree with the Office's assertion that Crystal anticipates making chimeric fiber proteins. Specifically, it is applicants' position that Crystal's express teachings are limited to complete fiber substitution (*i.e.*, Crystal's "5 base/7 fiber" vector (*See* Crystal, Example 2 at col. 23, line 60 through col. 24, line 54)), resulting in a chimeric ***capsid*** but not a chimeric ***fiber*** protein, as recited in the subject claims. Nevertheless, applicants agree with the Office that Crystal fails to teach a fusion fiber protein wherein the tail region of the fiber of the native, or first, serotype is retained and fused to the part of the non-native fiber, as recited in the subject claims.

The addition of the teachings of Wickham does not cure the failure of the proposed combination to teach each and every limitation of the subject claims. Wickham's teachings with respect to fiber chimeras in which the amino-terminal region of the native fiber is retained and operatively linked to the tropism-determining region of a fiber of another serotype are limited to the Ad5/Ad2 chimera of Example 1 and the Ad5/Ad3 chimera of Example 2. (Wickham, col. 11, line 43 through col. 12, line 62). In contrast, each of the subject claims recites the specific adenovirus serotype(s) from which the non-native part of each fiber chimera is obtained, none of which include serotypes 2 or 3. That is, claims 2, 3, 33, 34, 37, and 43-45 each recite that the non-native part of the fiber chimera is from a serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50. Similarly, claims 35, 36, 38-42, and 46-48 each recite that the non-native part of the fiber chimera is from serotype 35. The proposed combination of Crystal and Wickham advanced by the Office fails to teach or suggest this limitation of the subject claims and, accordingly, the Office has not established a *prima facie* case of obviousness

with respect to the subject claims. Applicants therefore respectfully solicit withdrawal of the rejection.

Lack of Motivation to Combine Reference Teachings

Furthermore, the Office has not identified any proper suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or combine reference teachings. When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. (*In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002)). The Office must make particular findings as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected the components for combination in the manner claimed. (*Id.* at 1343). These findings must extend to all material facts and must be documented on the record. (*Id.* at 1345).

It is stated in the Office Action: "One would have been motivated to [combine Crystal and Wickham] in order to receive the expected benefits of being able to efficiently interchange different receptor-binding domains from adenoviruses of different serotype, as taught by Wickham *et al.*, so as to easily and rapidly alter the tropism of the adenoviral vectors taught by Crystal *et al.*" (*Office Action*, page 6). At best, this is an improper "obvious to try" rationale and does not meet the requirements for a rejection under Section 103. (*See, e.g.*, MPEP § 2145X.A.). Neither Crystal nor Wickham suggest the desirability of combining each other's teachings, nor is there any other evidence of record to provide the requisite suggestion or motivation. The Office has made no particular findings based on evidence of record why, at the time the present invention was made, one of ordinary skill would have been motivated to select and combine Crystal and Wickham in the manner proposed. Accordingly, applicants respectfully submit the Office has not established a *prima facie* case of obviousness with respect to the subject claims and respectfully solicit withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 2, 3, 10, and 33-48 were rejected under the second paragraph of Section 112 as being indefinite. Specifically, the Office considers the subject claims to be vague and indefinite in that there is no clear definition provided in the specification as to what the term "N-terminus" encompasses. Applicants herein propose to amend claims 2, 33, 35, 37, 40, 43, and 46 to recite that the part of the fiber region of the second serotype is fused to the tail region of the native, or first, serotype, without any reference to "N-terminus".

Applicants respectfully submit the ordinarily skilled artisan, having knowledge of the structure of the fiber protein, including the orientation of the tail region and the remainder of the fiber protein (shaft and knob) in relation to one another, will have no difficulty understanding what is meant by the recitation in the subject claims that the part of the fiber protein of the second serotype is fused to the tail region of the serotype from which the vector was derived or, in some claims, the first serotype. Applicants thus respectfully submit the subject claims, as proposed to be amended here, are sufficiently definite as to meet the requirements of the second paragraph of Section 112. Accordingly, withdrawal of the rejection is respectfully requested.

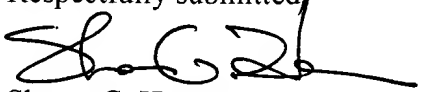
ENTRY OF AMENDMENTS

The proposed amendments to claims 2, 33, 35, 37, 40, 43, and 46 above should be entered by the Office because the amendments are supported by the as-filed specification and drawings and add no new matter to the application. Further, the amendments neither raise new issues nor require a further search. Finally, if the Office determines that the amendments do not place the application in condition for allowance, entry thereof is respectfully requested upon filing of a Notice of Appeal herein.

CONCLUSION

Claims 2, 3, and 33-48 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. If questions should remain after consideration of the foregoing that might be resolved by a telephone interview, the Office is kindly requested to contact applicants' undersigned representative, whose direct-dial telephone number is (801) 994-8719.

Respectfully submitted,



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Enclosure: VERSION WITH MARKINGS TO SHOW CHANGES MADE

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

2. (Six Times Amended) A recombinant vector derived from an adenovirus comprising at least one ITR and a packaging signal, the recombinant vector having a first insertion site for a nucleic acid sequence of interest, a second insertion site for functionally inserting a gene sequence encoding at least a part of a penton and/or hexon protein of a first adenovirus serotype, and a third insertion site for a gene sequence encoding a part of a fiber protein of a second adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50, a gene sequence encoding at least a part of a penton and/or hexon protein from the first adenovirus serotype inserted into the second insertion site, a gene sequence encoding the part of a fiber protein of the second adenovirus serotype inserted into the third insertion site, the gene sequence encoding the part of a fiber protein adapted to exhibit a desired tropism to a plurality of target cells in a host and fused to a tail region of a fiber of the adenovirus serotype from which the recombinant vector was derived[at its N-terminus].

33. (Twice Amended) A chimeric adenovirus comprising:

an adenoviral capsid derived from a first adenovirus serotype; and

a part of an adenoviral fiber derived from a second adenovirus serotype substituted for a corresponding part of a fiber of the capsid derived from the first adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50, wherein the part of the adenoviral fiber derived from the second adenovirus serotype is fused to a tail region of a fiber of the first adenovirus serotype[at its N-terminus].

35. (Twice Amended) A chimeric adenovirus comprising:

an adenoviral capsid derived from a first adenovirus serotype; and

a part of an adenoviral fiber derived from adenovirus serotype 35 substituted for a corresponding part of a fiber of the capsid derived from the first adenovirus serotype, the part of the adenoviral fiber derived from adenovirus serotype 35 fused to a tail region of a fiber of the first adenovirus serotype[at its N-terminus].

37. (Twice Amended) A method for producing a chimeric adenoviral particle having a capsid derived from a first adenovirus serotype exhibiting a desired tropism and antigenicity determined by a part of a fiber of a second adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50, the method comprising:

providing a recombinant vector derived from the first adenovirus serotype comprising at least one ITR, a packaging signal, an insertion site for a nucleic acid sequence of interest, and an insertion site for a gene sequence encoding a functional part of a fiber protein of the second adenovirus serotype;

inserting into the recombinant vector the gene sequence encoding the functional part of the fiber protein of the second adenovirus serotype, wherein the functional part of the fiber protein of the second adenovirus serotype is fused to a tail region of a fiber of the first adenovirus serotype[at its N-terminus];

transfecting said vector in a packaging cell; and

producing chimeric adenoviral particles.

40. (Twice Amended) A method for producing a chimeric adenoviral particle having a capsid derived from a first adenovirus serotype exhibiting a desired tropism and antigenicity determined by a part of a fiber derived from adenovirus serotype 35, the method comprising:

providing a recombinant vector derived from the first adenovirus serotype comprising at least one ITR, a packaging signal, an insertion site for a nucleic acid sequence of interest, and an insertion site for a gene sequence encoding a functional part of the fiber protein of adenovirus serotype 35;

inserting into the vector the gene sequence encoding the functional part of the fiber protein derived from adenovirus serotype 35, wherein the functional part of the fiber protein of the second adenovirus serotype is fused to a tail region of a fiber of the first adenovirus serotype[at its N-terminus];

transfecting said vector in a packaging cell; and

producing chimeric viral particles.

43. (Twice Amended) A recombinant vector derived from a first adenovirus serotype comprising:

at least one ITR;

a packaging signal;

a first insertion site for a nucleic acid sequence of interest;

a second insertion site for functionally inserting a gene sequence encoding a part of a fiber protein of a second adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50; and

a gene sequence encoding the part of the fiber protein of the second adenovirus serotype inserted in the second insertion site, the part of the fiber protein of the second adenovirus serotype exhibiting a desired tropism to a plurality of cells in a host and fused to a tail region of a fiber of the first adenovirus serotype[at its N-terminus].

46. (Twice Amended) A recombinant vector derived from a first adenovirus serotype comprising:

at least one ITR;

a packaging signal;

a first insertion site for a nucleic acid sequence of interest;

a second insertion site for functionally inserting a gene sequence encoding a part of a fiber protein of adenovirus serotype 35; and

a gene sequence encoding the part of the fiber protein of adenovirus serotype 35 inserted in the second insertion site, the part of the fiber protein of adenovirus serotype 35 exhibiting a desired tropism to a plurality of cells in a host and fused to a tail region of a fiber of the first adenovirus serotype[at its N-terminus].